

4. Conclusions

No studies are available that directly characterize health hazards and dose-response relationships for exposures to whole mixtures of benzene, toluene, ethylbenzene, and xylenes. All four components can produce neurological impairment, and benzene can additionally cause hematological effects which may ultimately lead to aplastic anemia and development of acute myelogenous leukemia. Concern for the carcinogenicity of BTEX is also raised by evidence that ethylbenzene is carcinogenic. No studies were located that directly examined joint toxic actions of mixtures of benzene, toluene, ethylbenzene, and xylenes on the nervous system, but additive joint action is plausible. Results of PBPK model simulations and experimental exposures with BTEX and ternary and quinary mixtures of its components (Haddad et al. 1999a, 1999b, 2000, 2001; Tardif et al. 1997) strongly suggest that joint neurotoxic action is expected to be additive at BTEX concentrations below approximately 20 ppm of each component. Neurotoxicity interaction studies of binary component mixtures support the plausibility of additive joint action at environmental levels of BTEX exposure. It is unclear whether the PBPK models are adequate for characterizing interactions from inhalation of BTEX mixtures above approximately 200 ppm of each component, or if the results are applicable to oral exposures. A component-based hazard index approach that assumes additive joint action and uses ATSDR MRLs based on neurological impairment is recommended for exposure-based assessments of possible neurotoxic health hazards from mixtures of BTEX. The possible hematotoxic and leukemogenic hazards of BTEX exposures should be evaluated on a benzene-specific basis because the other mixture components do not induce these effects. Considering the causal relationship between the noncancer hematological effects of benzene and development of leukemia, as well as lack of a cancer risk value for ethylbenzene, it is recommended that the inhalation cancer unit risk value for benzene be used to assess the benzene/ethylbenzene-related hematological/carcinogenic hazards from exposures to BTEX. Exposure to relatively high concentrations of BTEX (above approximately 20 ppm of each chemical) is expected to increase the potential for neurotoxicity and decrease the potential for hematotoxicity/carcinogenicity due to competitive metabolic interactions among the mixture components.